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NOTES UPON CARDIAC HYPERTROPHY.

BY

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I shall, I think, best satisfy you, and at the same time myself, if what I contribute to this evening's discussion takes the form of a series of notes upon the experimental pathology and the anatomy of cardiac hypertrophy, rather than that of an academic survey of the subject from the clinical standpoint. Frequently, it is true, I must of necessity illustrate what I have to say by reference to clinical history, but, on the whole, I shall leave the clinical aspects to be dealt with by those more capable.

In the first place, if we study the causes of hypertrophied heart, whether of hypertrophy of one or both sides, we see this that reading the clinical history of these cases the assigned causes of hypertrophy may be summed up under the heading of *increased work*. This one heading may be subdivided into three, increased work due to resistance from within, increased work due to resistance from without, increased work due to nervous stimulation and augmentor action. I shall not discuss this last subdivision, because frankly we are ignorant how far the hypertrophy that occurs in exophthalmic goitre and allied conditions is due to heightened blood pressure, and how far it is secondary to excitation of the accelerators or augmentors.

Of the increased resistance from within, or increased tension, the main causes are, heightened pressure in the arterial blood stream, and secondly, obstruction to the onward passage of blood within the heart itself, by stenotic diseases of one or other orifice. Of resistance from without, the one great cause is pericardial adhesion. To-night we have, as far as possible, to leave out the subject of valvular disturbance, and I shall neglect nervous disturb-

ances. There is still the large field of hypertrophy due to increased arterial pressure, and the pericardial adhesion. In all these cases, the individual fibres of the heart muscles of the affected regions have to contract under increased difficulty, they have to carry or contract against a greater load, and as a result of this, just as is the case with the skeletal muscles, with the muscles in the blacksmith's arm, and the muscles of the body in the all-round athlete, increased work brings about increased growth—brings about, that is to say, hypertrophy of the muscle.

Into the subject of the nature of this increased growth I shall enter in a few minutes' time, at present I wish to carry a word further this parallel between the behaviour of the cardiac and skeletal muscles, under circumstances in which the load is increased. If you take a skeletal muscle, for example, the gastrocnemius of the frog, so dear to the physiologist, and observe its contraction with gradually increasing loads, there are two points especially to be made out. In the first place the greatest amount of work is not performed with the smallest load, but there is a certain medium load with which the distance through which the load is pulled multiplied by the weight of the load gives the biggest result. This product of weight moved and the distance through which it is moved is the work done by the muscle. The most work, therefore, is done with a medium load. The second point is that with increasing weights fastened or brought to bear upon the muscle, that muscle in its resting state becomes more and more elongated, and with regularly increasing weights attached the shortening attained by the contracted muscle constantly diminishes. Or, to put the matter in a slightly different light, and to combine these two statements of fact, although with a certain medium load the greatest amount of work is done, nevertheless with that medium load the muscle in contracting does not attain to the same amount of shortening as it does with a lesser load.

Let me now apply these observations to what is found in the ventricular muscles of mammals. Experimentally

the amount of work performed by the ventricles of the mammalian heart can be increased by ligaturing the aorta with a sliploop ligature, and drawing this ligature more or less tight, according to need. [This in an animal that has been narcotised and curarised and subjected to artificial respiration, the heart being exposed by making a window in the ribs.] In such a case as this, as shown by Professor Roy and me,* the behaviour of the cardiac muscle can be observed and recorded by an apparatus, of which I give a rough diagram. (See Fig. 1.) The ends of this apparatus are attached to the surface, say of the left ventricle, by fine threads, and now it is possible to observe upon the recording drum the extent of contraction of the portion of muscle between the two points under different pressures within the heart. Narrow the aorta by drawing the ligature tight and the pressure is increased. Under these conditions it is found that the ventricular muscle reacts exactly along the same lines as does the gastrocnemius of the frog.

Similar results are obtainable if, instead of increasing the pressure in the arterial system by narrowing the aorta, we increase the work of the heart by increasing the amount of blood passing through it, either temporarily, by pressure upon the abdomen, whereby a large quantity of blood is expelled from the abdominal viscera, or by injecting into venous circulation some few hundred cubic centimetres of defibrinated blood. The results in all these cases are the same. By the instrument just described it is easy to see that the heart is more filled in diastole, so that the two ends of the levers are pushed further apart, and that in systole the ends do not approximate so nearly as in the condition when there is less resistance or less blood pouring through the organ.

It is seen from these observations that with increased pressure within the ventricle the wall expands in diastole. There is dilatation of the heart. But with the increased load to contract against the fibres do not shorten to the

* Heart beat and pulse wave. *Practitioner*, February, 1894, p. 81.

same extent; that is to say, with increased work of the heart there is, necessarily, accompanying the dilatation in diastole, a dilation in systole. All the blood is not expelled in systole. There is of necessity *residual blood*, as Roy and I termed it, in the ventricular chambers.

There is a general belief that the healthy heart, even

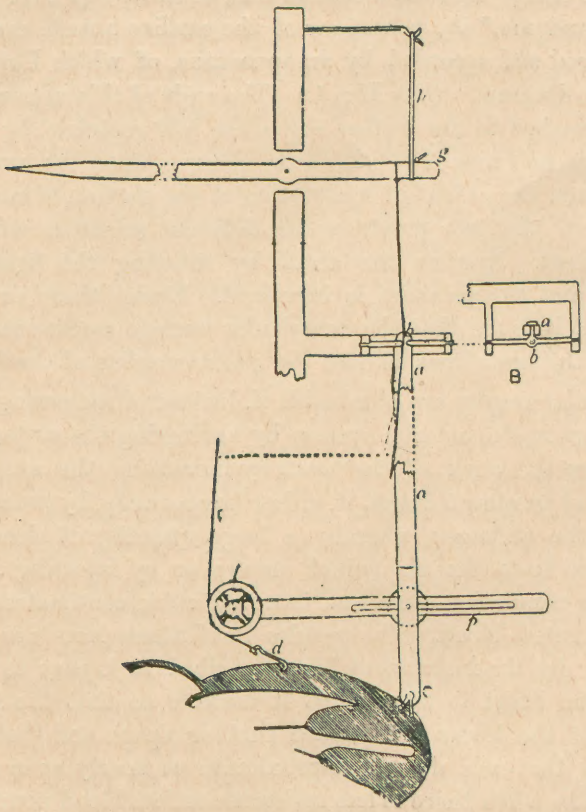


FIG. 1.—Myocardiograph for mammalian heart shown semi-diagrammatically. The light vertical rod *a*, which for convenience of space is shown shortened in the figure, is slung from the pivots which are represented in section as seen from above B. This arrangement allows the rod *a* to swing freely, the centre of rotation being the small hole at *b* (in B) The lower end, *c*, of this rod is fixed to the surface of the heart-wall as seen in the figure. To obtain tracings of the heart-wall, the small hook *d* is inserted in the visceral pericardium at a convenient distance from the end of the rod *a*. To this hook is attached a strong silken thread, *e*, which after passing round the light grooved pulley *f* is conveyed upwards through the small hole *b* to the lever *g*, being kept taut by the fine rubber thread *h*.

under conditions of increased work, contracts completely, so that the chamber is emptied at the end of systole. From what I have said it will be seen that this is not the case. One can go further and prove for one's self that even under ordinary conditions the mammalian heart does not completely expel all the blood within the ventricles. By taking a dog that has been curarised and subjected to artificial respiration, opening the chest wall, making an incision at the very apex of the left ventricle, so as just not to completely enter the cavity, then it is easy to push the little finger into the cavity through the thin apex without the loss of a drop of blood. The heart action is not recognisably disturbed by this procedure, and it can be felt that while the walls of the ventricle in the lower two-thirds up to the apices of the papillary muscles, close completely round the finger, there is a clear space in the upper third which is not and cannot be emptied of blood.

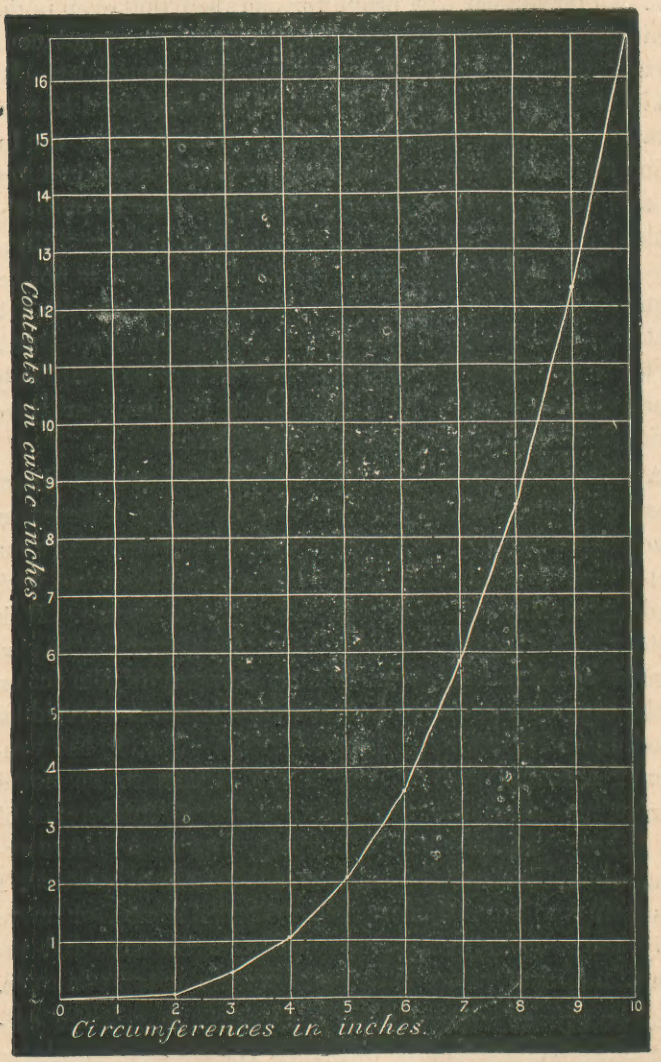
Although it may seem at first sight to have no direct bearing upon the subject of this evening's discussion, nevertheless it is worth while to make a few remarks upon this subject, inasmuch as it is so intimately associated with conditions of hypertrophy without valvular disease. It is quite possible that where there is increased work to be performed by the heart, there is some economy of the action of the organ when there exists a certain amount of residual blood, in and dilatation of the ventricles. Taking the ventricular chamber as a sphere,* there is this to be noted concerning the relationship between the circumference of the sphere and its contents, namely, that as a sphere expands its cubic contents increase out of all proportion, I was going to say, to increase in circumference, or more truly, the ratio between increase in cubic contents and increase in circumference is by no means an arithmetic ratio.

If the circumferences be taken as abscissæ, and the corresponding volumes as the ordinates, the curve of succesive

* The sphere is the nearest geometrical figure that can be employed here for purposes of illustration.

values is what is known to mathematicians as a cubical parabola. From this it follows that a degree of shortening of

Fig. 2.



Curve representing the relationship between the circumference of a sphere and ist volume, with successive unit increments of circumference.
Ordinates = volume in cubic inches.
Abscissæ = circumference in inches.

the fibres of the heart wall sufficient, let us say, to reduce the circumference of the ventricle one inch, will cause a greater diminution in *volume* (a greater output) the more dilated the ventricle is at the beginning of its contraction. For example, a diminution of the circumference by *one* inch of a sphere whose circumference is *ten* inches causes a diminution of the volume or an output, in the case of the heart, equal to *4.5* cubic inches, while a diminution by *one* inch in the circumference of a sphere *five* inches round causes a diminution or an output of only 1.027 cubic inches, although in the first case the circumference was reduced only by one-tenth, while in the other case it was reduced by one-fifth. That is to say, if we have a dilated heart the fibres will need to contract a very small amount, in order to expel a given amount of blood, compared with the amount they would have to contract in the normal undilated heart.

There are other factors to be taken into account, it is true, and Roy and I went a little into this subject in our paper published in the *Philosophical Transactions.** All that I wish to do here is to point out that it is possible that in a hard-working heart a certain amount of dilatation, with presence of residual blood, by diminishing the extent which each fibre is called upon to contract, may really be an economy to the organ as a whole.

It follows from these observations that *hypertrophy is never primary, dilatation always precedes hypertrophy.* This was recognized as most probable by Hilton Fagge; few other writers have laid stress upon the point. If, however, the heart muscle is well nourished, where this dilatation is due to increased work, by Paget's law hypertrophy ensues, and the numerical hypertrophy or hyperplasia of the ventricular muscle fibre will have the effect of lessening the load of each individual fibre. Consequently, with a lessened load, each fibre will contract more completely and the dilatation will tend to disappear. Where this is the case we have what is known as simple hypertrophy.

* Phil, Trans. of the Royal Society, London, 1892.

There can be no doubt that in the early stages, where ample reserve force and good compensation are present, this simple hypertrophy exists and may persist for years. But I would add that in the post-mortem room it is more rarely to be seen than is generally accepted. If a hypertrophied heart, say of Bright's disease, without valvular lesion, be examined within a few hours after death, in very many cases we appear to have this simple hypertrophy. If, however, time be given for the rigour and contraction of the muscle to pass off it is found—that at least is my experience—that the cavity of the left ventricle is distinctly larger than the cavity of the normal heart. I would say that only in those cases in which death has occurred from some intercurrent disease, and not from one of the cycle of diseases associated with cardiac hypertrophy—only when death occurs before the final stage of the disease of which cardiac hypertrophy is an integral part—do we obtain evidence of real simple hypertrophy. *Eccentric*, and not simple, hypertrophy is the rule ; that is to say, hypertrophy associated with definite dilatation of the ventricular cavities.

As for the concentric hypertrophy, which is said to be observable in non-valvular disease, I feel more and more assured that it is falsely so termed ; there is no such thing as true concentric hypertrophy, for the condition implies a lack of economy in the work of the organ, a most unnatural lack ; it implies that the ventrical in contracting expends a large part of its energy, after expelling the blood, in squeezing up the more internal fibres. Only within the last fortnight I obtained a specimen of so-called concentric hypertrophy. The patient, an old woman of eighty, in Dr. Stewart's ward at the Royal Victoria Hospital, died from cerebral apoplexy, following upon extreme atheroma of the aorta and the main vessels ; there was, in addition, atheromatous stenosis of the aortic valves, both conditions favouring the development of hypertrophy, with dilatation of the left ventricle.

The old woman had lingered some days in a comatose condition, with presumable lowering of the arterial blood pressure. In addition the tone of ventricular muscle had been in all probability considerably increased by digitalis. At any rate, at the autopsy a very few hours after death the left ventricle was found hypertrophied, and instead of being dilated was so firmly contracted that the only cavity left was immediately around the chordæ tendineæ. The thickness of the ventricular muscle at the junction of the lower and middle thirds was 20 mm.; that is to say, there was moderate hypertrophy. However, on coming to observe this heart the next day, the concentric hypertrophy had quite disappeared. With the passing off of rigidity there was a relatively large cavity left behind.

Where the left or right ventricle alone is affected the condition of the ventricle may be one of either simple or eccentric hypertrophy. Where, on the other hand, as Walshe noted more than thirty years ago, there is general hypertrophy of the organ, there hypertrophy is *always eccentric.*

A little consideration shows why this must inevitably be the case. So long as there is simple hypertrophy (hypertrophy without dilatation), so long the mitral valves remain competent, and there is no regurgitation into the left auricle, no increased work for that organ to do, no hypertrophy. So soon as the left ventricular muscle begins to fail and to be unable to contract properly under its load, dilatation ensues, and with this dilatation expansion or giving way of the muscular ring around the mitral orifice, and with this, relative incompetence of that orifice. It is only when this relative incompetence occurs, or when from other causes the mitral valves fail to perform their duty, that there is any possibility of the other chambers of the heart being called upon to do increased work. Thus it is that general hypertrophy of the heart demands or is associated with eccentric hypertrophy of the left ventricle.

Time forbids that I should go more fully into this subject or do more than point out that relative incompetence

of the auriculo-ventricular valves is more frequently found at the post-mortem than it is diagnosed during life. Relative incompetence, therefore, is not necessarily indicated by the presence of a murmur.

I cannot here enter fully into the histological nature of hypertrophy, although perhaps as a pathologist it might be expected that I should say some words upon this point. I will only say that while one can, in certain cases of hypertrophy, make out clearly that the individual fibres have undergone a definite increase in size, it is far more common to note, and of this there can be no doubt, that there has been an actual numerical increase in the fibres. This increase appears to be general throughout the ventricular wall and is possibly, nay probably, due not only to a new growth beneath the endocardium especially, but also to a splitting up or division of pre-existing fibres. It must be remembered that the heart muscle fibre is not a single cell, but is a compound, the result of a fusion of several cells into one individual unit. As a consequence of this it is possibly more easy for the fibres to split up into independent territories without undergoing temporary derangement of function than is the case with the cells of those tissues formed of isolated cell units.

To pass on now to certain aspects of this subject of hypertrophy more immediately in connection with this evening's discussion, I would point out that of the cases of hypertrophy without valvular lesion, we have to consider in the first place increased resistance through the column of blood. This could be brought about by increased amount of blood to be propelled, or, in the second, by increased resistance to passage in the arterial system. Of these two the first may exist as a constitutional condition, but the more one studies the less assured does one become that there is such a condition as general plethora unless these case be regarded as true plethora in which (as in German beer drinkers) there is oft repeated flushing of the circulation with imbibed fluid. Of increased resist-

ance in the arterial stream the reverse would appear to be the case, and with further studies of blood pressure in the arteries one begins to see that this plays an extremely important part. The hypertrophy following upon not only gouty conditions and senile artero-sclerosis, but also upon acute rheumatism, chorea and chlorosis may be present with or without lesion of the aortic or mitral valves of sufficient intensity to explain its extent; so that in all these cases we have to fall back upon increased blood pressure as a cause of hypertrophy.

Increased blood pressure in itself is capable of setting up a vicious circle of which one segment may be hypertrophy.

In the first place it leads to an increased nutrition of the walls of the arteries, increased nutrition leads to increased connective tissue growth of the walls, the increased fibrous tissue of the walls leads to contraction and increased rigidity of those walls, the increased rigidity leads to increased resistance to the passage of the blood current, the increased resistance required increased propulsive power on the part of the ventricular muscle, that is to say, increased work; the increased work of the heart leads to overgrowth and hypertrophy, and with this, heightened blood pressure and further increased nutrition of the walls. And now at last the stage is reached, this vicious circle continuing, in which either the walls give way or the heart.

The longer I study the pathology of the circulation—and during the last eight years I have given more time and thought to this than to any other branch of my subject—the more assured do I feel that increased blood pressure alone (however it be primarily brought about) is sufficient to explain the anatomical changes so constantly seen in arteries, valves and heart walls, without of necessity calling in chronic inflammation or specific agency. The changes I refer to are arterio-sclerosis, atheroma, and general fibroid thickening of the valves. Perhaps here again I am diverging from the main subject of this evening's discussion, but I say this as a connecting link with what I have just remarked and with what is about to follow.

While I am far from wishing to indicate that this is to be regarded as the sole cause of atheromatous and arterio-sclerotic changes, I hold that the changes I have mentioned can one and all be explained by the increased pressure within the vessels leading to an increased passage of fluid from the blood into the sub-endothelial layers of the intima, to an increased nutrition, and as a consequence to a proliferation of connective tissue in this region, which in itself as it contracts cuts off its own supply of nutrition, degenerates, and what is more, leads to degeneration of surrounding parts by cutting off their nutrition. The evil effects in arterio-sclerosis, with all its combined lesions, are not necessarily of an inflammatory origin.

Let us take now the hypertrophied heart. Time permits me to refer but briefly to the anatomical changes that may occur in it in the cases before us.

1. The overgrowth of the arterial walls may be associated with an increased tendency to the development of fibrous tissue in the immediate neighbourhood of the arteries, and thus a condition of so-called interstitial myocarditis may be set up; or

2. With an increased fibrosis of the arteries the narrowing of the channel may lead to incomplete nutrition of the territory supplied by each arterial twig, and as a consequence the muscle fibres at the periphery of the territory may be atrophied through lack of nutrition and be replaced by fibrous tissue. This is the so-called dystrophic sclerosis of the French school, and can frequently be seen more especially in the papillary muscles.

3. With the arterial disturbance there may be actual blocking of the atheromatous arteries, and so infarctous areas may originate, may undergo softening, may cause rupture of the heart or aneurism of the wall, or if the period of softening be successfully tided over, the replacement of the necrosed tissue leads to cicatricial development and disturbance of the normal contraction.

All these cases here mentioned inevitably cause interrup-

tion to the proper action of the remaining fibres and lead towards a final failure of the organ.

Another set of causes would seem to act along rather different lines, not so much of disturbances in the coronary arteries as disturbance in the quality of the nutrition, whereby the heart muscle tends to undergo fatty degeneration. In the uncomplicated case of hypertrophy, without valvular lesion, however, this fatty degeneration is rare; more frequent, according to the observations of Renaud, Browicz and Von Recklinghausen, there is a tendency for a sudden rupture of the heart fibres, from segmentation or fragmentation. It would seem as though, from the very careful observations of the last two, the weakened condition of the muscles permits some slight increase in the work done by the organ to bring about, not a local rupture, but a generalized separation of the fibres.

Possibly this segmentation may explain the suddenness of many cases of death in those with atrophied and dilated hearts. For my own part I cannot as yet see that it has been proved with absolute satisfaction that the fragmentation of the fibres is agonal or pre-agonal. Nor, looking back, does it seem to me that the most strongly marked cases that I have encountered of this fragmentation have been in cases of sudden death.

Lastly, to round off this paper, it is necessary to say a word concerning the hypertrophy that follows pericardial adhesion. Of this I may say that I cannot recall any case seen by me in which the hypertrophy was not markedly eccentric. Most frequently the hypertrophy has disappeared with, in its place, peculiarly extensive degenerative change.